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Health and Environmental Effects Profile for Trichloropropanes

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR TRICHLOROPROPANES

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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16. ABSTRACT

The Health and Environmental Effects Profile for trichloropropanes was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Existing data are insufficient to determine an Acceptable Daily Intake (ADI) or a carcinogenic potency factor for trichloropropanes.

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

ACKNOWLEDGEMENTS

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EXECUTIVE SUMMARY

The three isomeric trichloropropanes, namely 1,2,3-, 1,1,1- and 1,1,2-trichloropropanes, are liquid at room temperature. Very little information is available about 1,1,1- and 1,1,2-trichloropropane. The isomer 1,2,3-trichloropropane is used as a paint and varnish remover, solvent, and degreasing agent. The half-life for evaporation from water has been experimentally determined to be 56 minutes for 1,2,3-trichloropropane. The trichloropropanes are easily biodegraded by activated sludge.

Although trichloropropanes have been detected in a limited number of drinking waters and one surface water, enough ambient monitoring data are not available to permit an estimation of human exposure to this compound from inhalation and ingestion exposure routes.

Only limited toxicological information regarding trichloropropanes is available, and most of this information is on 1,2,3-trichloropropane. Liver microsomal enzymes isolated from rats were capable of interacting with 1,2,3-trichloropropane in the presence of NADP with an associated loss of cytochrome P-450 and the destruction of the heme moiety. In the process of enzymatic dechlorination, the soluble portion of a liver homogenate was essential, with little activity associated with purified microsomes. Most of the toxicity information is based on acute exposure, with 1,2,3-trichloropropane being the most toxic followed by 1,1,2- and 1,1,1-trichloropropane. This order of toxicity (as determined by LD_{50} values) was maintained with oral, dermal and inhalation exposure. Studies on the acute toxicity of 1,2,3-trichloropropane to dogs indicated that the major target organs are the central nervous system (depression), liver (necrosis) and kidney (necrosis and congestion). Russian investigations have suggested that chronic exposure to 1,2,3-trichloropropane at levels as low as 2.4

mg/m³ resulted in measurable changes in blood catalase and acetylcholinesterase activity. Subchronic exposure resulted in similar effects as well as a slight increase in the ploidy of liver cells; however, the toxicological importance of these changes is not readily apparent. In a preliminary study on the teratogenicity of 1,2,3-trichloropropane, slight maternal toxicity was observed but not fetotoxicity or terata. Recent mutagenicity assays of 1,2,3-trichloropropane suggest that the compound was mutagenic in the presence of a mammalian metabolic activation system; however, the toxicity of the compound to the Salmonella typhimurium tester strain makes the interpretation of these results less clear. Despite additional studies, sufficient information does not exist to draw a clear conclusion on the mutagenic hazard of trichloropropanes. There are no studies available to assess the carcinogenic potential of any of the trichloropropanes.

Aquatic toxicity data are available only for 1,2,3-trichloropropane. The results of a 7-day static renewal mortality assay with guppies (LC_{50} = 41.55 mg/ℓ) indicate that 1,2,3-trichloropropane is moderately toxic to fish. A calculated bioconcentration factor suggests that the potential for bioaccumulation is low.

1. INTRODUCTION

1,2,3-Trichloropropane is a colorless, clear liquid that is made by chlorinating propylene at low temperatures (25-40°C) (Hawley, 1981).

CAS Registry Number:	96-18-4
Formula:	$C_3H_5Cl_3$
Molecular Weight:	147.43 (Weast, 1972)
Melting Point:	-14.7°C (Weast, 1972)
Boiling Point:	156.85°C (Weast, (1972)
Density:	1.3889 at 20°C
Flash Point:	174°F (open cup) [TDB, 1981]
Vapor Pressure at:	2 torr at 20°C, 4 torr at 30°C (Verschueren, 1977)
Solubility at:	20°C: 1900 mg/ℓ (Dilling, 1977)
Log octanol-water Partition coefficient (Calculated):	2.63 (Koneman, 1981)
Production:	Probably >908 kg/year (SRI, 1975)

1,2,3-Trichloropropane is used as a paint and varnish remover, solvent, and degreasing agent (Hawley, 1981).

1,1,1-Trichloropropane

CAS Registry Number:	7789-89-1
Formula:	$C_3H_5Cl_3$
Molecular Weight:	147.43 (Weast, 1972)
Boiling Point:	106.5-108.5°C (Weast, 1972)
Density:	1.287 at 23°C (Weast, 1972)

1,1,2-Trichloropropane

CAS Registry Number:	598-77-6
Formula:	$C_3H_5Cl_3$
Molecular Weight:	147.43 (Weast, 1972)
Boiling Point:	140°C (Weast, 1972)
Density:	1.372 at 15°C

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

The air-water distribution coefficient for 1,2,3-trichloropropane, over a temperature range of 0-30°C, was measured by Leighton and Calo (1981). At 25°C, the distribution coefficient was determined to be 19.81. This relatively low distribution coefficient indicates that 1,2,3-trichloropropane cannot be stripped completely from water within a short (~10 minutes) purging time. The half-life for evaporation of 1,2,3-trichloropropane from 1 ppm aqueous solution in 6.5 cm solution depth and under 200 rpm stirring at 25°C in <0.2 mph air current was experimentally determined to be 56.1 minutes (Dilling, 1977). This result suggests that the evaporation of 1,2,3-trichloropropane from the aqueous phase into the atmosphere is one of the primary transport processes for this chemical.

The biodegradability of trichloropropane (isomer not specified) with activated sludge was studied by Matsui et al. (1975). Based on the efficiency of total organic carbon (TOC) removal, the half-life for biodegradation with activated sludge was determined to be ~4 hours from an initial trichloropropane concentration of 55 mg/ℓ.

The sediment sorption partition coefficient for 1,2,3-trichloropropane from aquatic media can be estimated from physical properties of the molecule. The organic carbon partition coefficient (K_{oc}) is first calculated from the octanol-water partition coefficient (K_{ow}) by correlation equations. The sediment sorption partition coefficient is then calculated from K_{oc} by the relation:

$$\text{Sorption partition coefficient} = \frac{K_{oc} \times \% \text{ organic carbon content}}{100\%}$$

Using a value of 2.63 for log K_{ow} (Koneman, 1981), log K_{oc} is calculated to be 2.37-2.81, depending on the correlation equation used (Briggs, 1981; Schwargenbach and Westall, 1981; Kenaga and Goring, 1980). This log K_{oc}

estimate is close to the experimental log K_{oc} value of 2.60 for tetrachloroethylene (Schwarzenbach and Westall, 1981). Thus, the sorption characteristics of 1,2,3-trichloropropane in aquatic media can be expected to be similar to that of tetrachloroethylene. It has been reported by Callahan et al. (1979) that tetrachloroethylene is not significantly sorbed to sediments containing low organic matter, whereas sediments rich in organic matter may show higher sorptive capacity. If a sediment organic content of 0.5% (typical of river sediment) is assumed, a sediment sorption partition coefficient of 1.18-3.21 is estimated for 1,2,3-trichloropropane, indicting a sediment concentration slightly greater than the water concentration, under equilibrium conditions.

The fate and transport of 1,2,3-trichloropropane in soil is difficult to predict from the available data. Based on the values of log K_{oc}, solubility and Henry's law constant for this compound and comparing with the corresponding values for tetrachloroethylene, (Verschueren, 1977) it can be predicted that this compound would have less volatility and more water leaching from soils than tetrachloroethyene. No prediction regarding the microbial degradability and chemical oxidation ability of this compound in soil can be made at the present time.

It should be emphasized that the fate of a chemical predicted from theoretical calculations, often may vary considerably from the experimental data. In the preceding discussions, the fate of 1,2,3-trichloropropane due to a few likely environmental processes has been predicted from theoretical equations only when experimental data were not available. However, extreme caution should be exercised when interpreting the predicted fate data based on theoretical calculations alone. No information was found regarding the environmental fate and transport of other trichloropropane isomers.

3. EXPOSURE

Drinking water from the Carrollton Water Plant in New Orleans, Louisiana was reported to contain <0.1 µg/ℓ of 1,1,1-trichloropropane and <0.2 µg/ℓ of 1,2,3-trichloropropane (Keith et al., 1976). The presence of 1,2,3-trichloropropane in Ames, Iowa drinking water also has been reported (U.S. EPA, 1976). Dewalle and Chian (1978) analyzed surface water from the Delaware River basin and detected trichloropropane (isomer unspecified) concentrations of >1 µg/ℓ in 3% of the samples. 1,2,3-Trichloropropane has also been found in the Rhine river near Lobith [Federal Republic of Germany (FRG)] at a mean and maximum concentration of 0.1 and 1.3 µg/ℓ, respectively (Bauer, 1981). This chemical has also been detected in the air of Bochum (FRG) at concentrations of 0.4 µg/m³ (Bauer, 1981). 1,2,3-Trichloropropane has not been detected in milk products, cosmetic products or cough mixtures, although it has been found in human renal capsul fat at a mean concentration of 3.12 µg/kg fresh weight (N=15) (Bauer, 1981).

Additional exposure data may be provided by a monitoring study reported in German (Bauer, 1981). This study (now being translated) looked at the concentration of 1,2,3-trichloropropane in various media in Germany; measurements were taken from samples of Rhine River water, drinking water, air, milk products, cosmetics, medicines (cough syrups), and human tissues (kidney, subcutaneous fat, lung, liver and muscle). Pertinent data will be added to this section as it becomes available.

No other monitoring data for the three isomers of trichloropropane could be found in the literature.

4. PHARMACOKINETICS

4.1. ABSORPTION

There was no specific information found in the literature searched on the absorption of the trichloropropanes; however, the observed toxicity of 1,2,3-trichloropropane indicates that absorption of this compound does occur following inhalation exposure.

4.2. DISTRIBUTION

Pertinent data regarding the distribution of the trichloropropanes were not located in the available literature.

4.3. METABOLISM

A few studies have been performed with the trichloropropanes to illustrate the enzymatic dechlorination of halogenated compounds by the liver. Van Dyke and Wineman (1971) used an *in vitro* system containing microsomes from rat liver and observed a 40% dechlorination of 1,1,2-trichloropropane during a 30-minute incubation. Although not performed with 1,1,2-trichloropropane, the reactions using other halogenated ethanes were dependent on the presence of NADP. In the model system using trichloroethane, the microsomal cytochrome P-450 enzyme system appeared to be neither rate-limiting nor essential to the dechlorination reaction, since washed microsomes had only 22% of the activity of microsomes supplemented with 1 mℓ of supernatant. By analogy, the results obtained with the ethanes were inferred to apply to the chloropropanes. However, further study is needed.

In a similar *in vitro* system Ivanetich et al. (1978) investigated the ability of 1,2,3-trichloropropane to interact and degrade microsomal enzymes. The microsomal enzymes were isolated from the liver of phenobarbital pretreated male Wistar rats and incubated at 30°C with 3.2 mM of 1,2,3-trichloropropane. Following incubation, it was determined by

difference spectrum and stimulation of CO-inhibitable NADPH oxidation that 1,2,3-trichloropropane participated in type I binding to cytochrome P-450. There was also a concommitant loss of cytochrome P-450, 15%, which was paralleled by a loss of the heme moiety. Cytochrome b_5 and NADPH-cytochrome C reductase were unaffected in this incubation system. As in the *in vitro* assay of the dechlorination of 1,1,2-trichloropropane, the interaction of 1,2,3-trichloropropane was dependent on the presence of an NADPH generating system. *In vivo* studies, however, failed to demonstrate an effect of 1,2,3-trichloropropane on liver microsomal enzymes (Moody et al., 1981). Male Sprague-Dawley rats received a single dose of 1,2,3-trichloropropane (180 mg/kg body weight) in mineral oil by intragastric intubation. The animals were killed 18 hours after treatment, and the levels in the liver of microsomal protein and RNA, phospholipid, NADPH cytochrome C reductase, cytochrome b_5 and chrome P-450 were determined. In all cases, the levels were similar in treated and control animals. The only biochemical parameter that was changed was the amount of some fatty acids with palmitic and linoleic acids slightly increased and stearic and arachedonic acids slightly decreased, while oleic and decosahexonoic acids remained the same as the controls. These results make it unclear whether the observed *in vitro* interactions of 1,2,3-trichloropropanes with microsomal enzymes also can occur *in vivo*.

4.4. EXCRETION

Pertinent data regarding excretion of trichloropropane isomers were not located in the available literature.

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of the trichloropropane isomers were not located in the available literature. However, 1,2,3-trichloropropane is being examined under the Carcinogensis Testing Program of the National Toxicology Program. Results from prechronic testing (14- and 120-day testing in mice and rats by gavage) should become available in mid-1983. The carcinogenicity bioassay itself remains to be scheduled. With no scheduling delays (and none are expected), final reports could be available as soon as early 1987.

5.2. MUTAGENICITY

Stolzenberg and Hine (1980) tested 1,2,3-trichloropropane (99% purity) for mutagenic activity using the standard Ames Salmonella plate test. Only one tester strain, TA100, was used in tests performed both in the presence and absence of a metabolic activation system (S9 mix derived from livers of Aroclor 1254 pretreated rats). At the two concentrations evaluated, a dose-dependent increase in revertant colony number was observed in the presence of S9 mix but not in its absence. At 1 µmole per plate 1120 revertants were reported and at 0.1 µmole per plate 141 revertants were found (background counts were subtracted from total revertant counts found). The authors indicated that the test material was "toxic to bacterial lawn growth." It is unclear, however, which treatment condition this refers to (i.e., with S9 mix or without S9 mix). Although, the test compound may be toxic, it appears to be mutagenic in the assay with S9 mix. Because of the inadequacies in reporting the results, these positive findings are not wholly unequivocal and should be confirmed by additional testing. More convincing evidence of mutagenicity in Salmonella would be the demonstration

of a dose-response using several concentrations ranging from 0.1-1 μmole/plate or up to a toxic concentration. It should be noted that in this study other halogenated hydrogenated hydrocarbons structurally-related to trichloropropane were found to be mutagenic when tested in Salmonella TA100. Therefore, this reinforces the concern that 1,2,3-trichloropropane is mutagenic in Salmonella. The brominated compounds, however, were generally more active than their chlorinated analogs.

Saito-Suzuki et al. (1982) assessed the ability of 1,2,3-trichloropropane (>99% purity) to cause dominant lethal mutations in SD male rats. Fifteen males were given 80 mg/kg/day of trichloropropane dissolved in olive oil by gastric intubation for 5 successive days. The authors concluded that there were no difference in the percent of postimplantation loss between the background control group and the treated groups. Also, no testicular lesions were found. It should be noted that the structurally-related chemicals 1,2,3-tribromopropane and 1,2-dibromo-3-chloropropane (which was used at a positive control) induced dominant lethals in this study. The negative findings for 1,2,3-trichloropropane do not support its nonmutagenicity. The dominant lethal assay is not considered a sensitive test for induced genetic damage (Russell and Matter, 1980).

According to Sidorenko et al. (1979), acute inhalation exposure (<168 hours) to 0.8 mg/ℓ 1,2,3-trichloropropane produced "changes in the short-term quality of chromosome sets in the direction of increasing cells of higher study"; these changes were determined in liver cells from "quantitative analysis of DNA." Further explanation was not provided.

Dominant lethal studies of 1,2,3-trichloropropane in SD rats showed no meaningful changes in the mean numbers of corpora lutea or in the numbers of implants, live embryos and dead implants (Saito-Suzuki et al., 1982).

Fifteen male rats were intubated on 5 successive days with 80 mg/kg/day of 1,2,3-trichloropropane (dissolved in olive oil), and every week for 8 weeks, each male was mated with a different untreated, virgin female.

In summary, there is insufficient information to draw a clear conclusion on the mutagenic hazard of trichloropropanes. The positive findings reported in bacteria and the fact that other structurally-related chemicals have been shown to be mutagenic support the need for further mutagenicity studies on this chemical. In addition to repeating the bacterial test, at least three additional assays should be conducted: one for gene mutations in an eukaryotic system, one for chromosomal aberrations and a test indicative of DNA damage (e.g., sister chromatid exchange or unscheduled DNA synthesis).

5.3. TERATOGENICITY

In a preliminary survey of workplace chemicals (Hardin et al., 1981), 1,2,3-trichloropropane was tested for teratogenic potential in Sprague-Dawley rats. Groups of 10-15 inseminated rats were administered the compound by intraperitoneal injection in corn oil at a dose of 37 mg/kg body weight. The treatments began on the first day of gestation and continued daily through day 15. On day 21, the rats were sacrificed and the fetuses were examined for abnormalities. Treatment with 1,2,3-trichloropropane resulted in maternal toxicity as indicated by either reduced body weight gain or altered weight in two or more organs; however, the specific changes observed in the animals treated with 1,2,3-trichloropropane were not enumerated. The treatment with 1,2,3-trichloropropane did not result in either fetal toxicity or teratogenesis.

5.4. OTHER REPRODUCTIVE EFFECTS

In the dominant lethal study previously described (see Section 5.2.), five daily doses of 80 mg/kg 1,2,3-trichloropropane did not affect the mating performance or reduce the frequency of fertile matings of SD rats (Saito-Suzuki et al., 1981). No testicular lesions were observed.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

The only information available in the literature searched on the effects of chronic exposure to 1,2,3-trichloropropane was a Russian abstract (Shaipak, 1976). In this study, male rats were exposed to an atmosphere containing 2.4 mg/m^3 of 1,2,3-trichloropropane for a "long time." Following cessation of exposure, the author observed alterations in central nervous sytem activity, and blood acetylcholinesterase and catalase activity. No specific information was available on the number of animals, length of exposure or degree of disruption of the above biological parameters.

The effects of exposure to 1,2,3-trichloropropane by inhalation for a period of 1 week have been studied by a group of Russian investigators. Belyaeva et al. (1974) exposed male albino rats to an atmosphere containing 0.8 mg/ℓ of 1,2,3-trichloropropane for 1 week followed by examination of the liver for increased ploidy as determined by the DNA content of individual cells. The exposure to 1,2,3-trichloropropane was associated with an increased percent (82.5 compared to 73.0%) of mononuclear tetraploid cells which the authors concluded resulted from the completion of a "complete wave of mitosis." In a more extensive follow-up study, Belyaeva et al. (1977) exposed groups (4-7 animals) of albino rats to 0.8, 2.16, 0.08 and 0.002 mg/ℓ of 1,2,3-trichloropropane, respectively, for 1, 1, 2 and 12 weeks. Exposure to the 2 higher concentrations for 1 week resulted in a similar increase in mononuclear tetraploid cells; however, the exposure to lower

levels for 2 or 12 weeks resulted in no statistical increases in tetraploid cells. According to the authors, these effects did not represent an appreciable toxic action by 1,2,3-trichloropropane.

In studies by Sidorenko et al. (1979), rats were exposed to 1,2,3-trichloropropane at concentrations between 2 and 800 mg/m³ for periods of 2 hours to 66 days. A linear concentration-time relation was observed between these exposure levels and time intervals for changes in blood catalase, acetylcholinesterase and the "total threshold indicator" (according to the authors, an indicator of central nervous system function) in the treated animals. Ambiguities in terminology and lack of description of experimental design make the toxicologic relevance of this study, particularly for the low-dose extended exposure groups, difficult to assess.

In a Russian inhalation toxicity study (Tsulaya et al., 1979), there was an indication that unspecified high concentrations of 1,2,3-trichloropropane, either alone or in combination with 1,2-dichloropropylene and perchloroethylene, stimulated desquamation and proliferation in the lungs of exposed rats and stimulated the macrophagal system. Exposure to mixtures were 7-86 days, with no strong evidence of synergistic interactions; the effects of combined exposures closely approached the sum of effects produced by individual components of the mixture.

5.6. ACUTE TOXICITY

Smyth et al. (1954, 1962) evaluated the acute toxicity of all the trichloropropanes in a series of range-finding studies. The oral LD_{50} was determined after a single intragastric intubation of five nonfasted Carworth-Wistar male rats, followed by a 14-day observation period. The LD_{50} for 1,1,1-, 1,2,3- and 1,1,2-trichloropropanes, respectively, were 7.46 and 0.32 mL/kg for the first two compounds, and 1.23 g/kg for the

last compound. Similar LD_{50} values of 0.369, 0.340, 0.380 and 0.505 g/kg were determined for 1,2,3-trichloropropane in mice, guinea pigs, rabbits and rats, respectively, by Shcherban and Pitenko (1976); however, in the abstract of this Russian study, the route of administration was not mentioned. Smyth et al. (1954, 1962) also determined the LD_{50} in rabbits following dermal penetration, and this value was >20, 1.77 and 14.1 mℓ/kg for 1,1,1-, 1,2,3- and 1,1,2-trichloropropane, respectively. The inhalation toxicity determined after 4 hours of exposure followed the same pattern with 1,1,1-trichloropropane killing 4 of 6 rats at 8000 ppm, 1,2,3-trichloropropane killing 5 of 6 rats at 1000 ppm and 1,1,2-trichloropropane killing 3 of 6 rats at 2000 ppm. Skin irritation and corneal injury were evaluated in rabbits on a scale of 1 (least severe) to 10 (most severe). The respective indices of skin and corneal damage were 4 and 2 for 1,1,1-trichloropropane, 1 and 4 for 1,2,3-trichloropropane, and 4 and 5 for 1,1,2-trichloropropane. A grade 6 for skin irritation indicated necrosis when undiluted compound was applied, and grade 5 for eye damage was considered severe with burns resulting from the application of 0.005 mℓ of the compound.

In a study of 1,2,3-trichloropropane for anthelmintic properties, Wright and Schaffer (1932) provided limited information on the symptoms of toxicity in dogs administered the compound. The three dogs were treated by gavage with 0.3 cc/kg body weight on 2 consecutive days or with a single dose of 0.2 or 0.5 cc/kg body. In all cases, the animals developed narcosis on the night following the last dose. The predominant signs of toxicity were swelling of cells in the liver with degradation of nuclei and associated necrosis, and congestion in the kidneys (with beginning signs of necrosis) and lungs. This study indicates that doses of 1,2,3-trichloropropane that result in severe central nervous system depression also cause degenerative changes in both the liver and kidney.

An abstract of a Russian inhalation toxicity study (Tsulaya et al., 1979) indicated that unspecified high concentrations of 1,2,3-trichloropropane, either alone or in combination with 1,2-dichloropropylene and perchloroethylene, stimulated desquamation and proliferation in the lungs of exposed rats, and stimulated the macrphagal (sic) system. Exposure to mixtures were for 7-86 days, with no strong evidence of synergistic interactions; the effects of combined exposures closely approached the sum of effects produced by individual components of the mixture.

5.7. OTHER RELEVANT INFORMATION

Silverman et al. (1946) assessed the sensory response of a group of 12 subjects to the vapors of 1,2,3-trichloropropane. After a 15-minute exposure, the majority of subjects estimated that a level of 50 ppm would be tolerable for an 8-hour exposure, but a concentration of 100 ppm was irritating to the eyes and throat but not the nose.

6. AQUATIC TOXICITY

6.1. ACUTE

A 7-day LC_{50} value of 41.55 mg/ℓ was determined for 1,2,3-trichloropropane in a static renewal assay with the guppy Poecilia reticulata (Könemann, 1981). In a 21-day assay with 1,2,3-trichloropropane, presumably done under the static renewal conditions, the amphipod Chaetogammarus marinus exhibited >50% mortality only when the trichloropropane concentration exceeded 18.00 mg/ℓ (Kooijman, 1981). Using the moving average method of calculation (Stephan, 1978), an LC_{50} of 14.7 mg/ℓ can be estimated by using interpolated data points from graphs in the article (Ward, 1983). Based on parametric analyses of results at concentrations of 0, 5.60, 10.00, 18.00, 32.00 and 56.00 mg/ℓ, Kooijman concluded "the observations indicated age-dependent mortality and non-normality of the threshold values".

6.2. CHRONIC

Information regarding the chronic toxicity of trichloropropanes was not located in the available literature.

6.3. PLANT EFFECTS

Regarding the effects of trichloropropanes on plants information was not located in the available literature.

6.4. RESIDUE

Specific information regarding residues of trichloropropanes in aquatic organisms is not available. Veith et al. (1980) have suggested, however, the use of the following equation to calculate bioconcentration factors (BCF):

$$\log BCF = 0.76 \log K_{ow} - 0.23$$

where K_{ow} is the partition coefficient between octanol and water. Using this equation and the log K_{ow} reported by Könemann (1981) for 1,2,3-trichloropropane (2.63), the BCF for whole fish was calculated to be 58.7.

6.5. OTHER RELEVANT INFORMATION

No other relevant information was found in the available literature.

7. EXISTING GUIDELINES AND STANDARDS

The American Conference of Governmental Industrial Hygienists (ACGIH, 1980) has recommended a threshold limit value (TLV) of 50 ppm (~300 mg/m³) and a short-term exposure limit (STEL) of 75 ppm (~450 mg/m³) for 1,2,3-trichloropropane. 1,2,3-Trichloropropane is regulated by the U.S. Department of Labor, Occupational Safety and Health Administration (OSHA). The current OSHA standard for this chemical is 50 ppm (~300 mg/m³) averaged over an 8-hour work shift.

8. APPROACHES TO RISK ASSESSMENT

The information on the toxicity of the trichloropropanes is limited; most of this information is related to acute exposure. The available literature on the toxicity after subchronic or chronic exposure lacks sufficient details in the number of animals exposed, the length of exposure and in the description of toxic effects elicited. Therefore, it is not possible to derive an acceptable daily intake (ADI) value for any of the trichloropropanes from studies on experimental animals. A TLV of 300 mg/m³ has been adopted by the ACGIH (1980) for 1,2,3-trichloropropane and could be considered as the basis for an ADI. In its documentation of this TLV, however, the ACGIH (1980) states that the TLV was derived by analogy to other (unspecified) chlorinated hydrocarbons due to their common property of hepatotoxicity. Because of the lack of chronic toxicity data and the general paucity of dose-response data for 1,2,3-trichloropropane, the derivation of an ADI from the TLV would be questionable and might require a large uncertainty factor. The TLV would correspond to a daily intake of 15.3 mg/kg, assuming that a 70 kg man breathes 10 m³ of air during an 8-hour workday and, in the absence of other information, that 50% of the chemical is absorbed. (This intake has also been modified by 5/7 to adjust from a 5-day work week to a 7-day week.) If an uncertainty factor of 100 were to be applied, the ADI would be 10.7 mg/day for a 70 kg man.

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